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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,607	01/30/2001	Ib Jonassen	4409-214-US	2082

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	11

DATE MAILED: 05/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/772,607	JONASSEN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/068,822* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Sequence Listing

1. Applicants' amendment to comply with sequence rule filed March 12, 2002 (Paper No. 10) is acknowledged, and CRF has been entered. A modified amino acid sequence, for example, GLP-1 derivative (page 6, lines 5-8 of specification) having Lys side chain modified with "N^{ε}-γ-Glu(Nα-tetradecanoyl)-OH" is cited as SEQ ID NO:2. However, the sequence listing indicates GLP-1 derivative without the modified side chain at Lys 28 is SEQ ID NO:2. Therefore, corrected amino acid sequences for SEQ ID NO:2 and other modified sequences in the sequence listing are required. Applicants must comply with the requirements of the sequence rules (37 CER 1.81-1.825) and provide a new copy of sequence listing and CRF containing all the sequences.

Election/Restrictions

2. Applicant's election with traverse of a species D), glucagon and glucagon-like peptide, and GLP-1 as the ultimate species in Paper No. 5 is acknowledged. Claims 1-19 have been cancelled, and new claims 20-46 have been added. The traversal is on the ground(s) that there would be no undue burden on the Examiner to examine all of the alleged species A) through X) of claims 1-19 since the examiner conducted an examination of the same claims for the parent application 09/068,822, and there is no lack of unity in the prosecution of PCT application. This is not found persuasive because the traversal is not on the grounds that the inventions are not independent and distinct, rather, the traversal is on the grounds that there is no additional search burden. Each peptide hormone with different amino acid sequence has different chemical property, produces different effect and has different utility, thus is patentably distinct.

Furthermore, coexamination of each of the additional peptide hormone would require search of the additional art area unnecessary for the examination of the elected peptide. Therefore, coexamination of each of these inventions would require a serious additional burden of search.

The restriction groups have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the invention is not coextensive particularly with regard to the literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other group. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist.

The requirement is still deemed proper and is therefore made FINAL.

Informalities

The disclosure is objected to because of the following informalities:

3. The specification is objected to because of the use of [...] in the text, e.g., "$Lys^{68}[N^{\varepsilon}$-γ-Glu(Nα-hexadecanoyl)-OH]-OH des (69, 70) human IGF-1" at page 5, line 24. Bracketing or underlining are commonly used to indicate amendments or changes in the claims as provided in 37 CFR 1.121(a)(2)(ii) and are normally not intended to be printed in the published patent (for detail see section below). Appropriate correction is required.

Claim Objections

4. Claim 33 is objected to because of the use of "His-Ala-.....Lys{N^{ε}-γ-Glu(Nα-tetradecanoyl)-OH]-OH. Bracketing or underlining are commonly used to indicate amendments or changes in the claims as provided in 37 CFR 1.121(a)(2)(ii) and are normally not intended to be printed in the published patent. For example, in claim 33, applicant has used "Lys{"N^{ε}-γ-Glu(Nα-tetradecanoyl)-OH]-OH" in such a manner that appears that the instant brackets would indicate deleted material and is thus, confusing as to whether the amino acid sequence in claim 33 would include "{N^{ε}-γ-Glu(Nα-tetradecanoyl)-OH" or not. The applicant can only amend by cancellation and presentation of a new claim. See also changes to 37 CFR 1.121 in Amendment rules package (Final Rule published on 8 Sep. 2000 (65 Fed. Reg. 54603), see also O. G. of 19 Sep. 2000 (1238 Off. Gaz. Pat. Office 77)). Claim 33 is also objected to because the claim cites an amino acid sequence but without a sequence identifier "SEQ ID NO:".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 20-26 and 34-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 20-26 and 34-40 are directed to a derivative of GLP-1 (or GLP-2), analog or fragment, wherein a lipophilic substituent optionally via a spacer is attached to the N-terminal

amino acid of GLP-1 (or GLP-2), analog or fragment, and wherein the lipophilic substituent is a straight chain fatty acid having "an amino group" and having 8-40 carbon atoms and the spacer is succinic acid, Glu or Asp. However, the specification indicates that when succinic acid is used as spacer, one of the carboxyl groups of succinic acid forms an amide bond with an amino group in the N-terminal amino acid of the peptide while the other carboxyl group forms an amide bond with an amino group contained in the lipophilic substituent; when Glu or Asp is used as spacer, one of the carboxyl groups in Asp or Glu forms an amide bond with an amino group in the N-terminal amino acid of the peptide while the amino group of Asp or Glu is attached to the acyl group of the lipophilic substituent (page 3, lines 4-20), which has no amino group, for example, the structures of lipophilic substituent and the spacer in claims 25, 26, 39 and 40 do not contain an amino group in the lipophilic substituent, the amino group in the structure belongs to Glu. Therefore, the specification has not shown how the fatty acid having an amino group as the lipophilic substituent is attached to the N-terminal amino acid of the peptide through Glu or Asp as the spacer, which is cited in claims 20 and 34. There is no disclosure indicating such compound has been made or used. Without guidance for the structure of fatty acid with an amino group as a lipophilic substituent attached to N-terminal amino acid of GLP-1 (or GLP-2) via Glu or Asp as a spacer, and for the condition of preparing the modified peptide, one skilled in the art would not know how to make and use of these peptides. Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 20-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-46 are indefinite because of the use of the term "a derivative of GLP-1 or analog or fragment thereof" or "a derivative of GLP-2 or analog or fragment thereof". The term "a derivative of GLP-1 or analog or fragment thereof" or "a derivative of GLP-2 or analog or fragment thereof" renders the claim indefinite, it is unclear how different the derivative is as compared to the parent compound, what amino acid sequence the analog or fragment of GLP-1 or GLP-2 has, and whether the analog or fragment of GLP-1 or GLP-2 is functional or not. Use of "a compound" instead of "a derivative" is suggested. Claims 21-26, 28-33, 35-40 and 42-46 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

7. Claim 25, for example, recites the limitation "$CH_3(CH_2)_rCO$-NHCH(COOH)$(CH_2)_2CO$-" in line 2. There is insufficient antecedent basis for this limitation in the claim because the lipophilic substituent does not have an amino group as indicated in the claim 20, the amino group in the structure belongs to Glu. See also claims 26, 39 and 40.

8. Claim 27, for example, is indefinite because of the use of the term "Glu-Lys wherein the Lys is attached to the C-terminal amino acid or Asp-Lys wherein the Lys is attached to the C-terminal amino acid". The term "Glu-Lys wherein the Lys is attached to the C-terminal amino acid or Asp-Lys wherein the Lys is attached to the C-terminal amino acid" renders the claim

indefinite, it is unclear whether the Lys is attached to the C-terminal amino acid of the GLP-1 or Asp-Lys. See also claim 41.

Conclusions

9. No claims are allowed.

Art of Record

The following references appear to be the closest art to the claimed invention. Wagner *et al.* (WO 95/03405) teach a method for producing a recombinant polypeptide such as GLP-2 having modification at Nα-terminus or C-terminus wherein the modification such as C-terminal amidation produces a polypeptide is longer acting and more potent than the naturally occurring polypeptide. However, Wagner *et al.* do not teach the modified peptide containing a lipophilic group. Muranishi *et al.* (J. Controlled Release 19, 179-188 (1992)) teach three modified peptide hormones such as thyrotropin-releasing hormone, tetragastrin and insulin having the fatty acid moieties (acyl chains) attached to their N-termini. However, the references do not teach the modified GLP-1 or GLP-2 having a lipophilic substituent optionally via a spacer attached to the amino acid at C-terminus, or having a lipophilic substituent optionally via a spacer attached to the amino acid at N-terminus, wherein the lipophilic substituent has an amino group and the spacer is succinic acid, Glu or Asp. Therefore, it appears the claimed invention is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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May 27, 2002

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER